REMARKS

Claims 7, 25-27, 38-41, and 49 were previously pending in this application. By this amendment, Claims 25, 26, 38, 39 and 49 have been amended to clarify that levels of UCP expression or activity in a cell wall, plasma membrane, or chloroplast are decreased, with respect to UCP expression or activity levels prior to decreasing the UCP expression or activity. Support for the amendment can be found throughout the specification as filed. As a result claims 7, 25-27, 38-41, and 49 are pending for examination with claims 7, 38, and 49 being independent claims. No new matter has been added.

Rejection under 35 U.S.C. §112, first paragraph

Written Description

The Examiner has rejected claims 26-27 and 39-41 under 35 U.S.C. §112, first paragraph as failing to comply with the written description requirement. Applicants respectfully traverse the rejection.

Applicants submit that sufficient information is provided in the specification as filed for one of ordinary skill in the art to conclude that Applicants were in possession of the claimed invention at the time of filing. The genus useful in the claimed methods includes UCP inhibitors. Applicants submit that not only does the specification provide numerous examples of UCP inhibitors, additional UCP inhibitors were known at the time of filing. Importantly, Applicants are not claiming the members of the genus of UCP inhibitors, but rather are claiming the use of members of this recognized genus in the methods claimed.

As a basis for the rejection of claims 26-27 and 39-41, the Examiner states on page 3 of the Office Action mailed 9/23/04, that the MPEP and the Revised Written Description Guidelines "teach that a demonstration of correlation between a structure and a function is *required* to adequately describe a broadly claimed genus" (emphasis added). The Examiner also suggests at page 3 that structures vary greatly and are only defined by a common function and that "Applicant has not described a common structural feature of the broadly claimed genus of UCP inhibitor that could be correlated with the claimed function of inhibition of UCP expression

or activity". Applicants respectfully disagree with the Examiner's interpretation of the Written Description requirement set forth in the Revised Written Description Guidelines.

The Written Description Guidelines state that, "whether the specification shows that applicant was in possession of the claimed invention is not a single, simple determination, but rather is a factual determination reached by considering a number of factors". The Guidelines then proceed to delineate factors that may be considered in a determination of whether there is sufficient evidence of possession. The factors that may be considered include: the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. The Guidelines do not select one of the features as determinative but rather cites the statement in Eli Lilly that a "disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient. (See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406). Applicants submit that identifying characteristics of the genus of UCP inhibitors for use in the invention as claimed are adequately described in the specification as filed, and that in light of the factors set forth by the court in Eli Lilly, and in the Written Description Guidelines, one of ordinary skill would recognize from the specification as filed that Applicants were in possession of the invention at the time of filing.

As set forth in the claims and described in the specification as filed, the claimed genus of inhibitors of UCP includes binding peptides, anti-UCP antibodies, UCP anti-sense nucleic acids, UCP dominant-negative nucleic acids, nucleotides, nucleotide analogs, tocopherols, and non-omega-3, -6 fatty acids. Numerous examples of members of this genus are known and used in the art as UCP inhibitors, although not in the claimed methods. The invention, in part, provides for the novel *use* of these inhibitors to regulate UCP expression or reduce UCP expression in specific locations of a plant, i.e. cell wall, cell membrane, or chloroplasts.

Applicants submit that based on the Written Description Guidelines, it is sufficient to have disclosed any combination of identifying characteristics of the genus, which are listed above herein, that distinguish the claimed invention from other materials and contend that this

has been done in the specification as filed. Applicants submit that the skill and knowledge of one of ordinary skill in the art combined with the clear description of the function of the members of the genus as UCP inhibitors and numerous examples of UCP inhibitors more than satisfies the criteria for written description set out in the Written Description Guidelines.

Applicants wish to point out that Applicants are not *claiming* the inhibitor molecules themselves, but rather are claiming the use of the genus of inhibitors to regulate or inhibit UCP activity in a plant cell wall or plasma membrane or chloroplast. Applicants submit that the Examiner's suggestion that each UCP inhibitor is expected to fit a common structure/function criteria is not applicable in the instant case as Applicants are not claiming the specific inhibitor molecules themselves. Instead, Applicants assert that the written description requirement is met in the instant case based on the combination of the high level of skill and knowledge in the art and the common function of the members of the genus, namely UCP inhibition. Applicants respectfully assert that based on the combination of these factors, one of ordinary skill in the art would conclude that Applicants were in possession of the claimed invention at the time of filing.

In addition, the Examiner states on page 3 of the Office Action mailed, 9/23/04, that "Applicant has not addressed the rejection of an adequate written description for UCP binding peptides and UCP antibodies in general comprising plant cell wall and plant plasma membrane UCP". The Examiner indicates at page 3 that Applicants have "only described commercially available antibodies that have been raised against mitochondrial UCP of non-plant origin". The Examiner appears to suggest that a UCP inhibitor of the claimed invention must be made specifically for recognition of plant cell wall and plant plasma membrane UCP and that the UCP inhibitors made or raised against other UCPs are not representative members of the claimed genus. Applicants assert that the ability of anti-UCP antibodies of non-plant origin to recognize UCP of plant origin has been demonstrated in the specification as filed. (see, for example, pages40 lines 24-30 and figs. 1-3.

The specification as filed supports Applicants' assertion that known UCP inhibitors are useful in the methods claimed. Applicants have provided in the specification at page 25, lines 7-21, an extensive list of some of the commercially available antibodies that are specific for UCP. Applicants have also demonstrated in the specification as filed that commercial anti-UCP

antibodies recognize and bind plant UCP, a point that is demonstrated by the use of anti-UCP2 antibody (Santa Cruz Biotechnologies) in Example 1.

Applicants submit that sufficient information is provided in the specification as filed for one of ordinary skill in the art to conclude that Applicants were in possession of the claimed invention at the time of filing, thus satisfying the written description requirement. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 26-27 and 39-41 under 35 U.S.C. §112, first paragraph.

Enablement

The Examiner has rejected claims 7, 25-27, 38-41 and 49 under 35 U.S.C. §112, first paragraph as lacking enablement. Applicants respectfully traverse the rejection.

With regard to the rejections on the basis that Applicants have not demonstrated the methods of the invention in a plant, Applicants respectfully disagree with the Examiner's conclusion. At page 11 of the specification as filed, Applicants clearly indicate that the term "plant" is to be interpreted in its broadest sense – and that it includes algae, e.g. *C. reinhardtii.* The specification indicates at page 9, line 17 through page 10, line 3, that *C. reinhardtii* has a cell wall and is used by those of skill in the art as a model for plant systems.

Applicants maintain that the claimed invention is enabled and that the Examiner has not performed a full analysis of the *Wands* factors as suggested under the law for enablement evaluations. Determination of undue experimentation follows from the analysis of the eight *Wands* factors. It appears that only some of these factors were considered by the Examiner; however, all of the factors should be considered for a proper analysis and a finding of non-enablement must be based on the evidence as a whole. *In re Wands* 858 F.2d 731, 737, 740, 8 U.S.P.Q.2d 1400, 1404, 1407 (Fed. Cir. 1988). Applicants maintain that full consideration of each and all of the *Wands* factors, in view of the state of the art at the time of filing, leads one to the reasonable conclusion that practicing the invention would not require undue experimentation.

The Examiner has considered the predictability of the art, although perhaps using an excessively stringent standard. In contrast to the Examiner's assertions of unpredictability of the use of inhibitors such as antisense compositions and antibody molecules to decrease activity or

expression of UCP, the predictability of the art as a whole for this aspect of the invention is high. One of ordinary skill in the art can reliably predict, make and test antisense nucleic acid molecules and other inhibitors as disclosed in the application and can also use the extensive list of described antibodies as inhibitors as described in the specification as filed. Numerous model systems (both cellular and whole organism) were available at the time of filing to test various aspects of inhibitor (e.g. antibody, antisense, etc) efficacy. For example, one can test the antibody or antisense compositions in plant cells, including *C. reinhardtii*, to determine the effect on expression or activity of a UCP gene, as well as to test the effect nutritional value, and resistance to infection. Whole plants also can easily be tested in a similar fashion. It is predictable from these and other possible routine experiments that one can determine the effect and/or efficacy of inhibitors of UCP in plants.

The Examiner has also considered the breadth of the claims, but Applicants do not agree with that the claims are overbroad. The claims are drawn to the use of known and readily identifiable compounds that inhibit expression or activity of UCP in plant cell wall, plasma membrane, or chloroplasts. Applicants have identified, for the first time, the presence of UCP activity outside of the mitochondria, and have determined that UCP inhibitors for the regulation of fuel metabolism in plants, production of nutritionally enhanced plants, and prevention of infections in plants. Applicants contend that broad scope is necessary to adequately protect the invention, which includes novel methods of using known UCP inhibitor molecules for the regulation of UCP activity and expression in plant cell walls, plasma membranes, and chloroplasts. Applicants submit that the claimed methods are not overly broad in scope when viewed in the context of the examples and models provided in the specification, coupled with the high level of knowledge and skill in the art.

The Examiner did not consider the remaining *Wands* factors: 1) existence of working examples, 2) guidance presented, 3) quantity of experimentation, 4) the nature of the invention, 5) the state of the prior art, and 6) the level of one of ordinary skill in the art. Applicants submit that none of these factors would weigh against a finding of enablement for the claimed invention. For example, very little experimentation is required to use inhibitor molecules to reduce the

expression or activity of UCP in a plant, once inhibitors and methods of contacting plants with the inhibitors are provided, as was done in the instant application.

Applicants maintain that adequate examples and guidance were provided. Applicants provided extensive descriptions of UCP sequences (see e.g., page 12), antisense nucleic acids (see, e.g., pages 21-22), binding peptides (see e.g., page 23-25), commercially available antibodies (see e.g., page25), and also describers nucleotide analogs, UCP dominant-negative nucleic acids, tocopherols, and non-omega-3, -6 fatty acids. The application as filed also provides methods to identify and make new inhibitors of UCP expression or activity.

Methods for testing the function of the inhibitor molecules were well known at the time of filing and Applicants cited several references which provide such methods and provides *C. reinhardtii* as an art-accepted model system. These descriptions provide sufficient guidance to one of ordinary skill in the art at the time of filing (in 2001) to use UCP inhibitors in the claimed methods. With respect to the working examples *Wands* factor, the court in *Wright* stated that "Nothing more than objective enablement is required, and therefore it is irrelevant whether this teaching is provided through broad terminology or illustrative examples." *In re Wright* at 1561 *citing In re Marzocchi* 439 F.2d 220, 223, 169 USPQ 367, 369 (C.C.P.A. 1971). Applicants have provided not only broad terminology which is readily understandable to one of ordinary skill in the art, but also illustrative examples in a model cell system as noted above. Thus the examples and guidance presented are not, by themselves, sufficient reasons to find undue experimentation.

The quantity of experimentation that would be required to practice the claimed invention is not excessive. Rather, the nature and quantity of such experimentation is completely routine in the relevant art. Selecting an inhibitor molecule, and testing the molecule for a decrease in the expression or activity of UCP and/or for the testing of the effect of an inhibitor on a plant's fuel metabolism, nutritional value, and resistance to infection are standard experimental procedures in plant molecular biology. For example, given the state of the art, one of ordinary skill in the art would only use routine experimentation to select and/or make a series of inhibitor molecules and test them in cells and/or plant systems. Based on the results obtained, additional rounds of

experimentation could focus on preferred molecules or variants having modified nucleotides as disclosed in the application. Such experimentation is routine as shown by the cited references and numerous other references publicly available at the time of filing of the application. Accordingly, any experimentation required would not be undue.

As described above, the claims are not excessively broad. Applicants have claimed the use of known inhibitors of UCP for the decrease in UCP activity or expression in plant cell wall, plasma membrane, or chloroplasts. The nature of the invention, inhibition of UCP activity and/or expression, is well known to one of ordinary skill in the art, although the applications proposed are novel.

The last two *Wands* factors are crucial to any determination of undue experimentation. In the *Wands* case, for example, the court's decision turned on the "high level of skill in the art at the time the application was filed", and that "all of the methods needed to practice the invention were known." *Wands* at 740, 8 USPQ2d at 1406. Applicants maintain that the same conclusions with respect to the state of the art and the level of skill in the art are true in the instant case, and therefore must weigh heavily in favor of a finding that undue experimentation is not required.

The level of skill in the art has an important effect on the amount of guidance which must be provided to enable the invention. As the court stated in *In re Howarth*, "[i]n exchange for the patent, [the applicant] must enable others to practice his invention. An inventor need not, however, explain every detail since he is speaking to those skilled in the art." *In re Howarth*, 654 F.2d 103, 105 (C.C.P.A. 1981). Thus the level of knowledge of one of ordinary skill in the art cannot be ignored in the *Wands* factor analysis. For the standard procedures contemplated in the application, the level of skill in the art is high. Applicants maintain that the person of skill in the art of plant molecular biology would know how to prepare, test and use UCP inhibitors in the claimed methods.

In summary, a full analysis of the *Wands* factors favors a conclusion that only routine experimentation would be required of one of ordinary skill in the art to practice the claimed invention throughout its scope.

Accordingly, Applicants respectfully request that the Examiner withdraw the rejections of claims 7, 25-27, 38-41 and 49 made under 35 U.S.C. §112, first paragraph.

Rejection under 35 U.S.C. §112, second paragraph

The Examiner has rejected claims 25, 26, 38, 39, and 49 under 35 U.S.C. §112, second paragraph as indefinite.

The Examiner indicates that claims 25, 26, 38, 39, and 49 lack a comparative basis for the use of the term "decreasing expression". Applicants submit that the comparative basis is inherent in the meaning of the word "decrease" when read in the context in the words of the specification and the claim. It would be clear to one of ordinary skill in the art that the "decrease" in expression or activity is a reduction from a first, pre-regulated level in the cell wall, plasma membrane, or chloroplast to a lower level in the cell wall, plasma membrane or chloroplast, respectively. In the interest of expediting allowance of the claims, Applicants have amended claims 25, 26, 38, 39, and 49 to further clarify the meaning claim language. Applicants submit that the claim amendments obviate the basis for the rejection and request the Examiner reconsider and withdraw the rejection of claims 25, 26, 38, 39, and 49 under 35 U.S.C. §112, second paragraph.

Rejection under 35 U.S.C. §102(b)

The Examiner has rejected claims 7, 25-27, 38-39, 41, and 49 under 35 U.S.C. §102(b) as anticipated by Kowaltowski, A.J., et al., FEBS Letters, 12998, Vol. 425; pages 213-216. Applicants respectfully traverse the rejection.

The Examiner states that "since the mitochondrial membrane is a part of a plant and has a plant plasma membrane, the Kowaltowski reference does anticipate the claimed invention". Applicants disagree with this conclusion for two reasons. First, the Examiner indicates that the mitochondria has a plant plasma membrane, which is an incorrect statement. The plasma membrane of a plant cell is the membrane that is inside the plant cell wall and surrounds the cytoplasm of the cell – it is the cell boundary. The mitochondrial membrane is a double-layer membrane, but is *not* the cell plasma membrane. Applicants submit that Kowaltowski et al. does not teach regulation of UCP expression and decreasing the expression or activity of UCP in a

plant cell wall, a plant plasma membrane, or plant chloroplast and therefore, Kowaltowski et al. does not anticipate the claimed invention.

In addition, the Examiner states at page 5 of the Office Action mailed 9/23/04 that the "only requirement for performing the methods of the claims is to contact the plant with a UCP inhibitor". Applicants submit that the Kowaltowski et al. reference does not teach or suggest contacting a plant with a UCP inhibitor. The methods described in the Kowaltowski include the inhibition of mitochondrial activity in suspensions of *isolated* rat liver and potato tuber mitochondria and the reference does not describe mitochondrial inhibition in a plant cell or a plant. Thus, Kowaltowski et al. does not teach regulation of fuel metabolism of a plant, which is an element of claim 7. Thus, Applicants submit that Kowaltowski et al. fails to teach every element of the claims and therefore does not anticipate the invention as claimed.

Applicants respectfully request the Examiner reconsider and withdraw the rejection of claims 7, 25-27, 38-39, 41, and 49 under 35 U.S.C. §102(b) as anticipated by Kowaltowski, A.J., et al., FEBS Letters, 12998, Vol. 425; pages 213-216.

Rejection under 35 U.S.C. §103(a)

The Examiner has rejected claims 7, 25-27, 38-39, 41, and 49 under 35 U.S.C. §103(a) as unpatentable over Kowaltowski, A.J., et al., FEBS Letters, 12998, Vol. 425; pages 213-216. Applicants respectfully traverse the rejection.

The Examiner states that the choice of antisense as an inhibitor of UCP activity would have been an obvious design choice because antisense inhibition is well known in the art.

There are three requirements that must be met to establish a *prima facie* case of obviousness. The Examiner must demonstrate that the reference teaches every element of the claimed invention, motivation to modify the teaching in the reference to make the claimed invention, and a reasonable likelihood of success in making the claimed invention. Applicants submit that these three requirements for a *prima facie* case of obviousness have not been met.

As described above herein, a mitochondrial membrane is a double-layer membrane, but is *not* the cell plasma membrane. Thus, although the Kowaltowski et al. reference describes the inhibition of mitochondrial activity, the reference does not teach regulation of UCP expression or

decreasing the expression or activity of UCP in a plant cell wall, a plant plasma membrane, or plant chloroplast. In addition, by virtue of the fact that the Kowaltowski et al. only describes methods of inhibition of mitochondrial activity with *isolated* mitochondria in suspension, the reference does not teach regulating fuel metabolism in a plant, which is also an element of claim 7. Because the Kowaltowski et al. fails to teach every element of the claims, even if it were combined with what is known in the art about antisense, the requirements to support a *prima facie* case of obviousness have not been met.

Accordingly, Applicants respectfully request the Examiner reconsider and withdraw the rejection of claims 7, 25-27, 38-39, 41, and 49 under 35 U.S.C. §103(a) as unpatentable over Kowaltowski, A.J., et al., FEBS Letters, 12998, Vol. 425; pages 213-216.

CONCLUSION

In view of the foregoing amendments and remarks, this application should now be in condition for allowance. A notice to this effect is respectfully requested. If the Examiner believes, after this amendment, that the application is not in condition for allowance, the Examiner is requested to call the Applicants' attorney at the telephone number listed below.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicants hereby request any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

Respectfully submitted,
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